Transcriptional profiles of circulating tumor cells reflect heterogeneity and molecular subtypes in advanced prostate cancer

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Abstract

BACKGROUND. New biomarkers for the detection and monitoring of aggressive variant prostate cancer (AVPC) including therapy-induced neuroendocrine prostate cancer (NEPC) are urgently needed, as measuring prostate-specific antigen (PSA) is not reliable in androgen-indifferent diseases.

METHODS. 102 blood samples from metastatic prostate cancer (mPC) patients, including 37 from histologically proven NEPC, were collected and CTCs were enriched using label-dependent and label-independent methods. Relevant transcripts indicative of androgen receptor pathway activation and neuroendocrine markers were selected for CTC profiling using semi-quantitative RT-PCR analysis and validated in published datasets and cell lines. Transcriptional profiles in patient samples were analysed using supervised and unsupervised methods.

RESULTS. CTC counts were increased in AVPC and NEPC as compared to metastatic hormone-sensitive prostate cancer (mHSPC). Gene expression profiles of CTCs showed a high degree of inter-patient heterogeneity, but NEPC-specific transcripts were significantly increased in patients with proven NEPC, while adenocarcinoma markers were decreased. Unsupervised analysis identified four distinct clusters of CTClow, ARhigh, amphicrine and pure NEPC gene expression profiles that reflected the clinical groups. Based on the transcript panel, NEPC could be distinguished from mHSPC or AVPC patients with a specificity of 95.5% and 88.2%, respectively.

CONCLUSION. Molecular subtypes of mPC can be distinguished by transcriptional profiling of CTCs. This PCR-based analysis can complement the monitoring of advanced PCa patients, allow detection of resistance to androgen receptor pathway inhibitors in blood samples and can be used as a research tool to validate basic research findings.

Do you have any conflicts of interest?

No, I do not have a conflict of interest.